Thrombosis: Anticoagulant Rivaroxaban soon also available for children

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Medicines can have different effects in children than in adults, which is not just a question of the right dose. Yet, still only few pharmaceuticals have been specifically tested and approved for this patient group. For treatment of thrombosis, children currently receive Heparin and Vitamin K antagonists which are problematic and not approved for children. A

recent international study investigate the anticoagulant Rivaroxaban approved for adults in children with acute venous thromboembolism. Comparing the efficacy and safety of Rivaroxaban to standard treatment children showed positive results. The study was headed by the pediatrician Christoph Male from the Department of Paediatrics at the MedUni Vienna. The study was published in the journal *Lancet Haematology*.

Development of pharmaceuticals for children has long been neglected, as there are many ethical and practical hurdles for the conduct of studies. Therefore, children frequently need to be treated with medicines not approved for this age group. Doses are estimated based on body weight and practical experience which carries the risk of a lack of effect or adverse effects, because children are not "small adults" and can react differently to pharmaceuticals.

The "EU Paediatric Regulation," in force since 2007, has the objective to improve the safety of medicines for children and adolescents. It requires that pharmaceutical manufacturers have to study medicines developed for adults also for treatment of children. An extensive clinical study program investigating Rivaroxaban as a medication for the treatment of venous thromboembolic in children has now been completed with the participation of MedUni Vienna. Rivaroxaban is a new agent for the inhibition of blood clotting administered orally. In contrast, Heparin has to be injected and its levels need to be frequently monitored in children by blood draws. Although thromboembolism is a hundred-fold less frequent in children than in adults, thrombosis occurs as secondary complications in severely ill children. For Vienna, approximately one hundred thrombosis cases are estimated per year.

The program underwent the three usual study phases for drug development. As prerequisite, an age-appropriate formulation for children was developed. Rivaroxaban can now be administered orally as

a liquid, which allows the accurate dosing and reliable administration even in young children and infants. In the initial study phases, suitable dosing regimens were determined for for the full range of ages and body weights of children. In the phase 3 study performed at the MedUni Vienna and a total of 107 international centers, 500 children aged between newborn age and 17 years suffering from acute venous thrombosis were treated by with Rivaroxaban or standard therapy. Principal investigator, Christoph Male: "The results showed at least equal efficacy and safety of Rivaroxaban compared to standard therapy. The results are also supported by the fact that they were comparable with study results from adult patients." The study results were presented as a late-breaking abstract at the Congress of the International Society of Thrombosis and Haemostasis in Melbourne in July 2019.

Reliable data for children

Rivaroxaban is expected to be approved for children in the EU in 2020 and will then also be available in the pediatric suspension. Christoph Male: "Finally, we have reliable data for the treatment of thrombosis in children. This was by far the largest study ever performed in this therapeutic area. In addition to its confirmed efficacy and safety, Rivaroxaban has a number of practical advantages particularly for children and will likely play an important role in their treatment in the future. We wish that all medicinal products would have such solid data for children ".

More information: Christoph Male et al. Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial, *The Lancet Haematology* (2019). DOI: 10.1016/S2352-3026(19)30219-4